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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,515	05/01/2002	Audrey Goddard	10466/300	8122

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KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/063,515	GODDARD ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0907*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 09/12/2007 has been entered. Claims 1–5 and 7–11 are pending and being examined.

Maintained Formal Matters, Objections, and/or Rejections:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1–5 and 7–11 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Afar (U. S. Publication No. 20050019870).

To the extent that "the polypeptide encoded by the cDNA deposited under ATCC accession number 209922" is, or is substantially similar to, "the polypeptide having the amino acid sequence of SEQ ID NO: 10", then applicant has the burden of distinguishing between anti-24P4C12 antibodies and the antibodies of claims 7–11, or alternatively, the antibodies of claims 7–11 are prima facie obvious over the prior art for the reasons given in the last Office action.

Applicants argue that:

> …the Afar reference does not expressly disclose an antibody which specifically binds to the polypeptide of SEQ ID NO:10, since the majority of 24P4C12 does not correspond to SEQ ID NO:10.

> Because Afar does not expressly disclose the claimed subject matter, Afar can anticipate the pending claims only if it inherently discloses an antibody that satisfies this claim. …the Afar reference inherently anticipates the claimed invention only if the answer to the following question is "yes": Does an antibody raised against 24P4C12 of Afar necessarily, always and without exception, possess the property of specifically binding to the polypeptide of SEQ ID NO:10? Applicants assert that the answer to this questions is clearly "No."
>
> …[because] amino acids 390-397 of Afar are not the same as amino acids 1-8 of SEQ ID NO:10. The Examiner has not established that there is any similarity between amino acids 1-397 of Afar and SEQ ID NO:10. Therefore, according to the Examiner's alignment, 397 of the 710 amino acids of 24P4C12 are apparently completely different from SEQ ID NO:10. That means that 56% of 24P4C12 differs from SEQ ID NO:10. Those of skill in the art recognize that as little as a single amino acid change can destroy binding specificity of an antibody to a target. …Clearly, antibodies raised against a protein with more than half of the amino acids being different from SEQ ID NO: 10 would not necessarily bind to the protein of SEQ ID NO: 10, when as little as a single amino acid change can destroy binding.
>
> …Afar generically discloses an antibody to 24P4C12, and does not disclose "antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12."
>
> …the [Kyte-Doolittle] plot makes clear that there are hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397. Therefore, the Kyte-Doolittle plot does not provide any basis for choosing to make antibodies only to amino acids 398-710 of 24P4C12. As such, antibodies to 24P4C12 do not necessarily bind to SEQ ID NO: 10, since 56% of 24P4C12 differs from SEQ ID NO: 10.
>
> In sum, Afar does not disclose any antibodies to any specific region of 24P4C12. Instead, there is merely a generic disclosure of antibodies to 24P4C12. While it is possible that an antibody to 24P4C12 would bind the polypeptide of SEQ ID NO:10, it is not a certainty since more than half of 24P4C12 apparently bears no similarity to SEQ ID NO: 10. Mere possibility is not sufficient for inherent anticipation: "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." M.P.E.P. §2112 ¶IV (8th ed. 2004), quoting In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added).

For the reasons discussed above, Afar does not teach each and every element of the claims, either expressly or inherently. As noted above, Afar generically discloses an antibody to 24P4C12, and does not disclose "antibodies that specifically bind epitopes in the 398-710 amino acid region of 24P4C12."

Even if it is obvious to make antibodies to hydrophilic regions, as discussed above, the Kyte-Doolittle plot makes clear that there are hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397. Therefore, the Kyte-Doolittle plot does not provide any basis for choosing to make antibodies only to amino acids 398-710 of 24P4C12. As such, antibodies to 24P4C12 do not necessarily bind to SEQ ID NO: 10, since 56% of 24P4C12 differs from SEQ ID NO: 10.

Applicants are unclear what the Examiner means by "modification," but to the extent the Examiner is referring to making antibodies exclusively to amino acids 398-710 of 24P4C12, this statement is without support.

Applicants respectfully request that the Examiner provide evidence to support this assertion, as Applicants believe that one of skill in the art would not recognize a motivation to make antibodies exclusively to amino acids 398-710 of 24P4C12 based on the cited reference and Kyte-Doolittle plot. The Examiner's unsupported assertion of fact represents a statement by "official notice." See, e.g., In re Zurko, 258 F.3d 1379, 1385, 59 USPQ2d 1693, 1697 (Fed. Cir. 2001); and In re Ahlert, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970). Applicants submit that the Examiner's statement asserted by official notice is not well-known or capable of instant and unquestionable demonstration as being well-known. To the contrary, one of skill in the art would conclude that the plot clearly shows hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397. Thus, in accordance with M.P.E.P. §2144.03C, Applicants respectfully request documentary evidence demonstrating that one of skill in the art would recognize a motivation to make antibodies exclusively to amino acids 398-710 of 24P4C12 based on the cited reference and Kyte-Doolittle plot. If this is not what was meant by the Examiner's statement that "[o]ne of skill in the art would be motivated to make this modification," Applicants request that the Examiner clarify to what "modification" he is referring.

A generic disclosure of antibodies to an entire protein is not a disclosure of antibodies to a specific region. Absent some motivation to make antibodies exclusively to amino acids 398- 710 of 24P4C12, the disclosed antibodies to 24P4C12 clearly do not inherently possess the claimed features. Because the cited reference does not disclose each and every

> element of the claims, either expressly or inherently, the Examiner has failed to establish a prima facie case of obviousness. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-5 under 35 U.S.C. § 103(a) as obvious over Afar et al.

Applicants' arguments have been fully considered but they are not persuasive. Afar readily identifies regions of the 24P4C12 protein that show immunogenic structure and discloses antibodies to those regions. Based on the Kyte-Doolittle plot, Afar clearly identifies immunogenic regions that are identical to the immunogenic regions in applicants' SEQ ID NO: 10 and clearly discloses antibodies to those identical immunogenic regions. The examiner is aware that a genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. See MPEP § 2131.02. Therefore, in view of Afar's clear identification and disclosure of immunogenic regions in 24P4C12 that are identical to the immunogenic regions in applicants' SEQ ID NO: 10, the arguments that "56% of 24P4C12 differs from SEQ ID NO:10", that "amino acids 390-397 of Afar are not the same as amino acids 1-8 of SEQ ID NO:10", that the "Examiner has not established that there is any similarity between amino acids 1-397 of Afar and SEQ ID NO:10", and that "there are hydrophilic regions throughout the entire length of 24P4C12, including amino acids 1-397" are of no consequence.

Unlike the findings of the court in *In re Zurko*, in the present case and in the present rejection the examiner does not rely on any alternative references to reach a conclusion of obviousness. Nor does the examiner rely on any general conclusions about what is "basic knowledge" or "common sense" to one of ordinary skill in the art to reach a conclusion of obviousness. Rather, the examiner has pointed to concrete evidence in the record to support the conclusion of obviousness. Specifically, Afar concretely states that regions of the 24P4C12

protein that show immunogenic structure can readily be identified using various methods known in the art, such as Kyte-Doolittle (page 34, full paragraph 3). The examiner has provided a Kyte-Doolittle plot to show that it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to identify hydrophilic regions in the 24P4C12 structure and to make anti-24P4C12 antibodies that recognize the hydrophilic regions with a reasonable expectation of success. Anti-24P4C12 antibodies that specifically bind epitopes in the 398–710 amino acid region of 24P4C12 will also specifically bind SEQ ID NO: 10 because this region of 24P4C12 is identical to amino acids 34–321 of SEQ ID NO: 10. One of ordinary skill in the art would be motivated to make this modification in order to detect 24P4C12 in prostate samples. The invention is prima facie obvious over the prior art. The Kyte-Doolittle plot is not a reliance on assessment of basic knowledge and common sense not based on any evidence in the record and, lacking substantial evidence support. Nor is the examiner's conclusion of obviousness based on some hypothetical realm of the examiner's understanding or experience. To the contrary, the Kyte-Doolittle plot provides sufficient support for the conclusion that the claimed antibodies are obvious.

Unlike the findings of the court in *In re Ahlert*, applicants, though given [in the Patent Office] the opportunity, do not challenge the correctness, notoriety or repute of the Kyte-Doolittle plot. Furthermore, the Kyte-Doolittle plot is concretely supported by Afar at page 34, full paragraph 3. However, applicants' do not challenge the fact that regions of the 24P4C12 protein that show immunogenic structure can readily be identified using various methods known in the art, such as Kyte-Doolittle (Afar, page 34, full paragraph 3). Therefore, the ability of one of ordinary skill in the art to readily identify regions of the 24P4C12 protein that show

immunogenic structure must be considered conclusive. Therefore, one of ordinary skill in the art could have readily predicted immunogenic regions in the 398–710 amino acid region of 24P4C12 and could have readily made antibodies to those regions. Anti-24P4C12 antibodies that specifically bind epitopes in the 398–710 amino acid region of 24P4C12 will also specifically bind SEQ ID NO: 10 because this region of 24P4C12 is identical to amino acids 34–321 of SEQ ID NO: 10.

If one is to argue, as applicants have argued, that an antibody raised against 24P4C12 of Afar does not necessarily, always and without exception, possess the property of specifically binding to the polypeptide of SEQ ID NO:10 because amino acids 390-397 of Afar are not the same as amino acids 1-8 of SEQ ID NO:10 and it has not been established that there is any similarity between amino acids 1-397 of Afar and SEQ ID NO:10, then one must also accept the argument that an antibody raised against the immunogenic regions of amino acids 398-710 of 24P4C12 of Afar necessarily, always and without exception, possess the property of specifically binding to the polypeptide of SEQ ID NO:10 because amino acids 398-710 are identical to amino acids 9-321 of SEQ ID NO: 10. Because Afar clearly identifies the immunogenic regions of 24P4C12 with reference to Kyte-Doolittle and clearly discloses antibodies that bind those regions, Afar clearly identifies antibodies that bind the immunogenic regions of amino acids 398-710 of 24P4C12.

It is noted for the record that SEQ ID NO: 10 is a partial amino acid sequence and that applicants have not established any dissimilarity between the undisclosed portion of the polypeptide that comprises SEQ ID NO: 10 and amino acids 1-397 of Afar's 24P4C12 other than

the difference between amino acids 1-8 of SEQ ID NO: 10 and amino acids 390-397 of Afar's 24P4C12.

The examiner fails to see the significance of the references that allegedly disclose that as little as a single amino acid change can destroy binding specificity of an antibody to a target because the rejection is not over antibodies that bind epitopes that differ between SEQ ID NO: 10 and 24P4C12. Rather, the rejection is over antibodies that bind immunogenic regions in 24P4C12 that are identical to immunogenic regions in SEQ ID NO: 10.

The examiner also considers applicants' arguments somewhat misleading because the examiner never stated that one skilled in the art would only choose to make antibodies to amino acids 398-710 of 24P4C12 or that one skilled in the art would make antibodies exclusively to amino acids 398-710 of 24P4C12. Nor does the examiner consider such an exclusive teaching necessary in order for Afar to anticipate the claimed antibodies because, as discussed above, a reference that clearly names the claimed species anticipates the claim no matter how many other species are named. Nor does the examiner consider such an exclusive teaching necessary in order for Afar to render the claimed antibodies obvious because, as discussed above, antibodies raised against the immunogenic regions of amino acids 398-710 of 24P4C12 would specifically bind the polypeptide of SEQ ID NO:10 because amino acids 398-710 are identical to amino acids 9-321 of SEQ ID NO: 10. The argument that "[a] generic disclosure of antibodies to an entire protein is not a disclosure of antibodies to a specific region" is illogical because in making antibodies one makes antibodies that bind specific regions of a protein. As discussed above, Afar clearly identifies the immunogenic regions of 24P4C12 with reference to Kyte-Doolittle and clearly discloses antibodies that bind those regions. The Kyte-Doolittle plot clearly

identifies immunogenic regions of amino acids 398-710 of 24P4C12. Afar would have yielded predictable, obvious results to one of ordinary skill in the art at the time of applicants' invention. Specifically, Afar clearly identifies antibodies that bind the immunogenic regions of amino acids 398-710 of 24P4C12. Because amino acids 398-710 of 24P4C12 are identical to amino acids 9–321 of SEQ ID NO: 2, Afar clearly identifies antibodies that specifically bind SEQ ID NO: 10.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, MANJUNATH RAO, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID ROMEO/
PRIMARY EXAMINER
ART UNIT 1647

DSR
NOVEMBER 20, 2007